**DOCKET NO.:** ISIS-4976 **PATENT**
**Application No.:** 10/038,335
**Office Action Dated: November 29, 2004**

**In the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

Please cancel claims 11-13.

8. (Original) A method for inhibiting the division of a malignant mammalian cell comprising contacting said malignant mammalian cell with a chemically modified oligonucleotide having no more than about 27 nucleic acid base units, said oligonucleotide having the sequence $(N_xG_{3-4})_QN_X$ wherein X is 1 to 8 and Q is 1 to 6, wherein said oligonucleotide modulates mammalian telomere length.

9. (Original) The method of claim 8 which is carried out *in vitro*.

10. (Original) The method of claim 8 which is carried out *in vivo*.

Claims 11-13 (cancelled)

14. (previously presented) A chemically modified oligonucleotide having no more than about 27 nucleic acid base units, said oligonucleotide having the sequence $(N_xG_4)_QN_X$ wherein X is 1 to 8 and Q is 1 to 6.

15. (previously presented) The oligonucleotide of claim 14 which has at least one phosphorothioate linkage.

16. (previously presented) The oligonucleotide of claim 14 which has at least one 2' modification of a sugar of said oligonucleotide.

17. (previously presented) The oligonucleotide of claim 14 which is a chimeric oligonucleotide.

18. (previously presented) The oligonucleotide of claim 14 wherein said chemical modification is:

a backbone modification selected from the group consisting of chiral phosphorothioate, phosphorodithioate, phosphotriester, aminoalkylphosphotriester, methyl phosphonate, 3'-alkylene phosphonate, 5'-alkylene phosphonate, chiral phosphonate, phosphinate, phosphoramidate, thionoalkylphosphonate, thionoalkylphosphotriester, selenophosphate, boranophosphate, morpholino, siloxane, sulfide, sulfoxide, sulfone, formacetyl, thioformacetyl, methylene formacetyl, thioformacetyl, riboacetyl, alkene containing backbone, sulfamate, methyleneimino, methylenehydrazino, sulfonate, sulfonamide, and amide; or

a modified 2' sugar moiety selected from the group consisting of F, N-alkyl, O-alkenyl, S-alkenyl, N-alkenyl, O-alkynyl, S-alkynyl, N-alkynyl, O-alkyl-O-alkyl, $C_1$ to $C_{10}$ lower alkyl, substituted lower alkyl, alkenyl, alkynyl, alkaryl, aralkyl, O-alkaryl, O-aralkyl, SH, $SCH_3$, OCN, Cl, Br, CN, $CF_3$, $OCF_3$, $SOCH_3$, $SO_2CH_3$, $ONO_2$, $NO_2$, $N_3$, $NH_2$, heterocycloalkyl, heterocycloalkaryl, aminoalkylamino, polyalkylamino, and substituted silyl, wherein the alkyl, alkenyl and alkynyl may be substituted or unsubstituted $C_1$ to $C_{10}$ alkyl or $C_2$ to $C_{10}$ alkenyl and alkynyl; or

a modified nucleobases selected from the group consisting of 5-methylcytosine, 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-methyl adenine, 6-methyl guanine, 2-propyl adenine, 2-propyl guanine, 2-thiouracil, 2-thiothymine, 2-thiocytosine, 5-halouracil, 5-holocytosine, 5-propynyl uracil, 5-propynyl cytosine, 6-azo uracil, 6-azo cytosine, 6-azo thymine, 5-uracil, 4-thiouracil, 8-halo guanine, 8-amino guanine, 8-thiol guanine, 8-thioalkyl guanine, 8-hydroxyl guanine, 8-halo adenine, 8-amino adenine, 8-thiol adenine, 8-thioalkyl adenine, 8-hydroxyl adenine, 5-halo uracil, 5-bromo uracil, 5-trifluoromethyl uracil, 5-halo cytosine, 5-bromo cytosine, 5-trifluoromethyl cytosine, 7-methylguanine, 7-methyladenine,

2-F-adenine, 2-amino-adenine, 8-azaguanine, 8-azaadenine, 7-deazaguanine, 7-deazaadenine, 3-deazaguanine, 3-deazaadenine, phenoxazine cytidine(1H-pyrimido(5,4-b)(1,4)benzoxazin-2(3H)-one), phenothiazine cytidine (1H-pyrimido(5,4-b)(1,4)benzothiazin-2(3H)-one), substituted phenoxazine cytidine (e.g. 9-(2-aminoethoxy)-H-pyrimido(5,4-b)(1,4)benzoxazin-2(3H)-one), carbazole cytidine (2H-pyrimido(4,5-b)indol-2-one), pyridoindole cytidine (H-pyrido(3',2':4,5)pyrrolo(2,3-d)pyrimidin-2-one), 7-deaza-adenine, 7-deazaguanosine, 2-aminopyridine, and 2-pyridone.

19. (previously presented) The oligonucleotide of claim 18 wherein the 2' sugar modification is $-O-CH_2CH_2OCH_3$, $-O(CH_2)_2ON(CH_3)_2$, $-O-CH_2-O-CH_2-N(CH_2)_2$, $-O-CH_3$, $-OCH_2CH_2CH_2NH_2$, $-CH_2-CH=CH_2$), -F, $-O((CH_2)_nO)_mCH_3$, $-O(CH_2)_nOCH_3$, $-O(CH_2)_nNH_2$, $-O(CH_2)_nCH_3$, $-O(CH_2)_nONH_2$, or $-O(CH_2)_nON((CH_2)_nCH_3))_2$, where n and m are from 1 to about 10.

20. (previously presented) The oligonucleotide of claim 14 wherein said oligonucleotide modulates mammalian telomere length.

21. (previously presented) A chemically modified oligonucleotide having no more than about 27 nucleic acid base units, said oligonucleotide having the sequence $(N_xG_4N_y)_Q$ or $(G_4N_xG_4)_Q$ wherein X is 1 to 8, Y is 1 to 8, and Q is 1 to 4, wherein said oligonucleotide modulates mammalian telomere length.

22. (previously presented) The oligonucleotide of claim 21 which has at least one phosphorothioate linkage.

23. (previously presented) The oligonucleotide of claim 21 which has at least one 2' modification of a sugar of said oligonucleotide.

24. (previously presented) The oligonucleotide of claim 21 which is a chimeric oligonucleotide.

25. (previously presented) The oligonucleotide of claim 21 wherein said chemical modification is:

a backbone modification selected from the group consisting of chiral phosphorothioate, phosphorodithioate, phosphotriester, aminoalkylphosphotriester, methyl phosphonate, 3'-alkylene phosphonate, 5'-alkylene phosphonate, chiral phosphonate, phosphinate, phosphoramidate, thionoalkylphosphonate, thionoalkylphosphotriester, selenophosphate, boranophosphate, morpholino, siloxane, sulfide, sulfoxide, sulfone, formacetyl, thioformacetyl, methylene formacetyl, thioformacetyl, riboacetyl, alkene containing backbone, sulfamate, methyleneimino, methylenehydrazino, sulfonate, sulfonamide, and amide; or

a modified 2' sugar moiety selected from the group consisting of F, N-alkyl, O-alkenyl, S-alkenyl, N-alkenyl, O-alkynyl, S-alkynyl, N-alkynyl, O-alkyl-O-alkyl, $C_1$ to $C_{10}$ lower alkyl, substituted lower alkyl, alkenyl, alkynyl, alkaryl, aralkyl, O-alkaryl, O-aralkyl, SH, $SCH_3$, OCN, Cl, Br, CN, $CF_3$, $OCF_3$, $SOCH_3$, $SO_2CH_3$, $ONO_2$, $NO_2$, $N_3$, $NH_2$, heterocycloalkyl, heterocycloalkaryl, aminoalkylamino, polyalkylamino, and substituted silyl, wherein the alkyl, alkenyl and alkynyl may be substituted or unsubstituted $C_1$ to $C_{10}$ alkyl or $C_2$ to $C_{10}$ alkenyl and alkynyl; or

a modified nucleobases selected from the group consisting of 5-methylcytosine, 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-methyl adenine, 6-methyl guanine, 2-propyl adenine, 2-propyl guanine, 2-thiouracil, 2-thiothymine, 2-thiocytosine, 5-halouracil, 5-holocytosine, 5-propynyl uracil, 5-propynyl cytosine, 6-azo uracil, 6-azo cytosine, 6-azo thymine, 5-uracil, 4-thiouracil, 8-halo guanine, 8-amino guanine, 8-thiol guanine, 8-thioalkyl guanine, 8-hydroxyl guanine, 8-halo adenine, 8-amino adenine, 8-thiol adenine, 8-thioalkyl adenine, 8-hydroxyl adenine, 5-halo uracil, 5-bromo uracil, 5-trifluoromethyl uracil, 5-halo cytosine, 5-bromo cytosine, 5-trifluoromethyl cytosine, 7-methylguanine, 7-methyladenine, 2-F-adenine, 2-amino-adenine, 8-azaguanine, 8-azaadenine, 7-deazaguanine, 7-deazaadenine, 3-

deazaguanine, 3-deazaadenine, phenoxazine cytidine(1H-pyrimido(5,4-b)(1,4)benzoxazin-2(3H)-one), phenothiazine cytidine (1H-pyrimido(5,4-b)(1,4)benzothiazin-2(3H)-one), substituted phenoxazine cytidine (e.g. 9-(2-aminoethoxy)-H-pyrimido(5,4-b)(1,4)benzoxazin-2(3H)-one), carbazole cytidine (2H-pyrimido(4,5-b)indol-2-one), pyridoindole cytidine (H-pyrido(3',2':4,5)pyrrolo(2,3-d)pyrimidin-2-one), 7-deaza-adenine, 7-deazaguanosine, 2-aminopyridine, and 2-pyridone.

26. (previously presented) The oligonucleotide of claim 25 wherein the 2' sugar modification is $-O-CH_2CH_2OCH_3$, $-O(CH_2)_2ON(CH_3)_2$, $-O-CH_2-O-CH_2-N(CH_2)_2$, $-O-CH_3$, $-OCH_2CH_2CH_2NH_2$, $-CH_2-CH=CH_2$), -F, $-O((CH_2)_nO)_mCH_3$, $-O(CH_2)_nOCH_3$, $-O(CH_2)_nNH_2$, $-O(CH_2)_nCH_3$, $-O(CH_2)_nONH_2$, or $-O(CH_2)_nON((CH_2)_nCH_3))_2$, where n and m are from 1 to about 10.